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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/856,850	09/19/2001	Waltraud Ankenbauer	5304	4731

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EXAMINER	
KIM, YOUNG J	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 06/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/856,850	ANKENBAUER ET AL.	
	Examiner	Art Unit	
	Young J. Kim	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 5-7 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 5-7 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 January 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office Action responds the Amendment received on March 29, 2004.

Preliminary Remark

Claims 1-4 and 8-17 have been canceled. Claims 5-7 are pending and are under prosecution.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5-7 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a Written Description Rejection.

The claims are drawn to a composition comprising a first thermostable enzyme exhibiting 3'-5' exonuclease activity but essentially no DNA polymerase activity and a second enzyme exhibiting DNA polymerase activity.

Claims encompass a composition comprising a genus of thermostable enzyme exhibiting 3'-5' exonuclease activity but essentially no DNA polymerase activity, wherein said genus encompasses thermostable enzyme exhibiting said characteristics which are of different origins and species. However, the specification provides a single species of a recombinant *Afu*

exonuclease III (page 7, specification) produced by the process disclosed on pages 14-15 of the instant specification.

Therefore, the specification provides insufficient written description to support the genus encompassed by the claim.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of the recombinant *Afu* exononuclease III, the skilled artisan cannot envision the detailed chemical structure of the encompassed enzymes, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The sequence itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmacentical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.
>
> An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel*, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.
>
> The name cDNA is not itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA. Describing a method of preparing a cDNA or even describing the protein that the cDNA encodes, as the example does, does not necessarily describe the cDNA itself. No sequence information indicating which nucleotides constitute human cDNA appears in the patent, as appears for rat cDNA in Example 5 of the patent. Accordingly, the specification does not provide a written description of the invention of claim 5.

It is also noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that:

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

Therefore, only the composition comprising only the recombinant *Afu* exonuclease III, but not the full breadth of the claim (or none of the sequences encompassed by the claim) meets the written description provision of 35 USC 112, first paragraph. The single species specifically disclosed cannot be representative of the genus. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 5-7 are rejected under 35 U.S.C. 102(b) as being anticipated by Zhu et al. (Nucleic Acids Research, 1991, Vol. 19, No. 9, page 2511).

Preliminarily, the instant rejection is being reinstated because the instant specification discloses that a thermostable enzyme of the instant invention is preferably active at, "70°C to 80°C" (page 4, 2nd paragraph). Therefore, Applicants' arguments received on November 26, 2003, stating that because the enzyme of Zhu et al. is inactivated at, "95°C for five minutes," (page 4, 2nd paragraph, Response) cannot be sustained as the instant specification clearly state that the thermostable enzyme of the instant invention is preferably active at, at least 70°C. Since there is no evidence to the contrary that the enzyme of Zhu et al. is not active at, at least 70°C, Zhu et al. would clearly anticipate the instant claims.

Zhu et al. disclose a method of using the combination of exonuclease III and polymerase in a PCR (Polymerase Chain Reaction) (Abstract).

The exonuclease employed by Zhu et al. is added in an effort to reduce contamination during PCR (therefore, arguably enhances PCR fidelity) (1st column). Protocol 1 discloses that Taq polymerase (claim limitation 7) and Exo III (1st enzyme with essentially no polymerase activity) are present in a PCR mixture (therefore, a composition).

Therefore, Zhu et al. anticipate the invention as claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 5-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barnes et al. (US 2003/0049643 A1).

Barnes et al. disclose a well-known advantage provided by using a polymerase having a 3'-5' exonuclease activity in combination with another polymerase (Abstract; [0039]). Barnes et al. disclose that the proof-reading activity provided by a polymerase having the 3'-5' exonuclease activity (such as *Pfu* polymerase) in conjunction with a polymerase such as *Taq* polymerase, allowing for higher fidelity of larger amplified products [0008].

Barnes et al. identify a polymerase having the 3'-5' exonuclease activity as being, "E2" and a polymerase having the polymerase activity as, "E1." [0062].

Barnes et al. do not explicitly disclose a mixture of an enzyme having a 3'-5 exonuclease activity but essentially no polymerase activity and a polymerase exhibiting DNA polymerase activity.

Barnes et al. disclose that the enzymatic activity value in the minor E2 component **is the 3'-exonuclease activity, not the DNA polymerase activity** and that in fact, the artisans state that it is, "further believed that this DNA **polymerase activity** is potentially troublesome, leading to unwanted synthesis or less accurate synthesis under conditions optimized for the majority E1 DNA polymerase" [0072-0073].

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to arrive at the claimed invention for the following reasons.

Barnes et al. disclose a well-known advantage of using a combination of a DNA polymerase and another polymerase with 3'-5 exonuclease proof-reading activity, which generates a higher fidelity amplification product (*ut supra*), as well as providing such mixture [0011].

While Barnes et al. is silent on whether one of the enzymes of the mixture, that is, the enzyme having 3'-5' exonuclease activity, has essentially no DNA polymerase activity, one of ordinary skill in the art would have been clearly motivated to make such a modification based on the motivation provided by Barnes et al., who states that the DNA polymerase activity in the enzyme having 3'-5' exonuclease activity might be potentially troublesome, leading to unwanted synthesis or less accurate synthesis under conditions optimized for the enzyme having the DNA polymerase activity [0072-0073].

Therefore, based on such statement, one of ordinary skill in the art would have been clearly motivated to modify the enzyme having the 3'-5' exonuclease activity so that its DNA polymerase activity would be minimized or eliminated to arrive at the claimed invention with a reasonable expectation of success.

Double Patenting – Maintained

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

The provisional rejection of claims 5-7 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 3 of copending Application No. 10/192,902 (filed July 11, 2002; published as US 2003/0119150 A1, published June 26, 2003), made in the Office Action mailed on January 30, 2004 is maintained for the reasons of record.

Applicants' arguments presented in the Amendment received on March 29, 2004 have been fully considered but they are not found persuasive for the following reasons.

Applicants argue that when a provisional double patenting rejection is the only rejection remaining in the application, the examiner should withdraw that rejection and permit the application to issue as a patent (citing MPEP 822.01).

Such argument is moot in view of the rejections provided in the instant Office Action under sections 35 U.S.C. 102(b) and 103(a).

Therefore, the rejection is maintained for the reasons of record.

Conclusion

No claims are allowed.

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Young J. Kim whose telephone number is (571) 272-0785. The Examiner can normally be reached from 8:30 a.m. to 6:00 p.m. Monday through Thursday. If attempts to reach the Examiner by telephone are unsuccessful, the Primary Examiner in charge of the prosecution, Dr. Kenneth Horlick, can be reached at (571) 272-0784. If the attempts to reach the above Examiners are unsuccessful, the Examiner's supervisor, Gary Benzion, can be reached at (571) 272-0782. Papers related to this application may be submitted to Art Unit 1637 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant does submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office. All official documents must be sent to the Official Tech Center Fax number: (703) 872-9306. For Unofficial documents, faxes can be sent directly to the Examiner at (517) 273-0785. Any inquiry of a

general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-0507.

Young J. Kim
Patent Examiner
Art Unit 1637
6/8/04

yjk